

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

Art Unit: 1647

NICO CERLETTI

Examiner: D. Romeo

APPLICATION NO: Not Yet Assigned

FILED: Herewith

FOR: NEW PROCESS FOR THE PRODUCTION OF BIOLOGICALLY
ACTIVE PROTEINAssistant Commissioner for Patents
Washington, D.C. 20231PRELIMINARY AMENDMENT

Sir:

Kindly enter the following preliminary amendment prior to calculating the filing fee for the application.

IN THE SPECIFICATION

At page 1, between lines 1 and 2, insert— This is a continuation of U.S. Application No. 09/316,724, filed 5/21/99, which is a continuation of U.S. Application No. 08/776,444, filed 1/24/97 (now abandoned).

IN THE CLAIMS

Delete claims 1-18. Add the following claims 19-25.

19. Process for the production of a dimeric, biologically active Transforming Growth Factor type $\beta 2$ (TGF- $\beta 2$) or $\beta 3$ (TGF- $\beta 3$), or a salt thereof, comprising treating the denatured monomeric form of said TGF- $\beta 2$ or $\beta 3$ with a folding buffer comprising an organic solvent selected from the group consisting of DMSO (Dimethylsulfoxide), and DMF (Dimethylformamide) and a mixture thereof, said buffer additionally containing glutathione in its reduced form; thereby permitting folding of the monomeric TGF- $\beta 2$ or $\beta 3$ into the spatial conformation which after dimerization is associated with the biological activity, while retaining said monomer in a soluble form; the process being conducted in the substantial absence of either a chaotropic agent or a copper or manganese salt.